Amendments to the claims:

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. (***original***) Isolated sulfenyl amide cysteine-containing protein, or a homologue, allelic form, species variant, derivative or mutein thereof.

2-94. (***cancelled***)

95. (***new***) Isolated protein sulfenyl amide according to claim 1 which is characterized by the HC(X5)R signature motif, or a homologue, allelic form, species variant, derivative or mutein thereof.

96. (***new***) Isolated protein sulfenyl amide according to claim 1 which is PTP sulfenyl amide, or a homologue, allelic form, species variant, derivative or mutein thereof.

97. (***new***) A process for screening for an inhibitor of a protein capable of forming a sulfenyl amide as defined in claim 1, which process comprises the steps of: (a) providing a sulfenyl amide of the protein (or a homologue, allelic form, species variant, derivative or mutein thereof); (b) contacting the sulfenyl amide of step (a) with a test compound; and (c) determining whether the test compound binds to the sulfenyl amide.

98. (***new***) A process according to claim 97 further comprising the step of (d) identifying the test compound as an inhibitor on the basis of its ability to prevent or inhibit the reductive activation of the sulfenyl amide to active protein.

99. (***new***) The process of claim 98 for producing a pharmaceutical composition further comprising the step of: (e) incorporating the inhibitor identified in step (d) into a pharmaceutical excipient.

100. (***new***) A method of reducing the activity of a protein tyrosine phosphatase (PTP), the PTP being one which is convertible between an active form and an inactive form, the inactive

form being characterized by the presence of a sulfenyl amide moiety formed at the active site of the PTP between the sulfur atom of a cysteine group and a backbone nitrogen atom of a neighbouring amino acid, whereby the sulfenyl amide moiety distorts and inactivates the active site of the PTP and wherein the sulfenyl amide moiety is disruptible to restore the inactive form of the PTP to the active form thereof;

which method comprises inhibiting disruption of the sulfenyl amide moiety, or modifying the sulfenyl amide moiety to prevent restoration of the inactive form of the PTP to the active form.

101. (*new*) The method according to claim 100 wherein the sulfenyl amide moiety is disruptible by reaction with a reducing agent to restore the inactive form of the PTP to the active form thereof.

102. (*new*) A method according to claim 100 wherein the sulfenyl amide moiety is disruptible to regenerate the cysteine group.

103. (*new*) A method according to claim 100 which comprises inhibiting disruption of the sulfenyl amide moiety by means of a ligand that binds to the inactivated active site of the PTP.

104. (*new*) A method according to claim 100 which comprises modifying the sulfenyl amide moiety to prevent restoration of the inactive form of the PTP to the active form.

105. (*new*) A method according to claim 104 which comprises reversibly modifying the sulfenyl amide moiety.

106. (*new*) A method according to claim 104 which comprises irreversibly modifying the sulfenyl amide moiety.

107. (*new*) A method according to claim 104 in which the sulfenyl amide moiety is modified by reaction with a nucleophilic ligand.

108. (*new*) A method according to claim 107 wherein the sulfenyl amide moiety is modified by reaction with a nucleophilic ligand having a nucleophilic group that will react with the

sulfenyl amide moiety, and a binding region for binding to the PTP sulfenyl amide in the region of the sulfenyl amide moiety.

109. (***new***) A method according to claim 108 wherein the nucleophilic group is selected from the group consisting of a thiol, disulfane, primary thioamide, secondary thioamide, primary thiourea, secondary thiourea, primary amine, secondary amine, primary hydrazine, secondary hydrazine, primary hydrazide, secondary hydrazide, primary hydrazone, secondary hydrazone, primary amide, secondary amide, primary urea, secondary urea, primary sulfonamide, secondary sulfonamide, 5-membered ring heterocycle containing NH, alcohol, hydroxylamine, oxime, hydroxamic acid, carboxylic acid, sulfoxide, sulfate and a nitrone.

110. (***new***) A crystal of sulfenyl amide protein tyrosine phosphatase 1B.

111. (***new***) A computer system containing either (a) atomic coordinate data according to Table 1 or Table 2 ± root mean square deviation from the Cα atoms of not more than 1.5Å, said data defining the three-dimensional structure of sulfenyl amide protein tyrosine phosphatase 1B or at least selected coordinates thereof; (b) structure factor data (where a structure factor comprises the amplitude and phase of the diffracted wave) for sulfenyl amide protein tyrosine phosphatase 1B, said structure factor data being derivable from the atomic coordinate data of Table 1 or Table 2 ± root mean square deviation from the Cα atoms of not more than 1.5Å; (c) atomic coordinate data of a target sulfenyl amide protein tyrosine phosphatase protein generated by homology of the target based on the data of Table 1 or Table 2 ± root mean square deviation from the Cα atoms of not more than 1.5Å; (d) atomic coordinate data of a target sulfenyl amide protein tyrosine phosphatase protein generated by interpreting X-ray crystallographic data or NMR data by reference to the data of Table 1 or Table 2 ± root mean square deviation from the Cα atoms of not more than 1.5Å; or (e) structure factor data derivable from the atomic coordinate data of (c) or (d).

112. (***new***) Computer readable media with at least one of: (a) atomic coordinate data according to Table 1 or Table 2 ± root mean square deviation from the Cα atoms of not more than 1.5Å recorded thereon, said data defining the three-dimensional structure of sulfenyl amide protein tyrosine phosphatase 1B, or at least selected coordinates thereof; (b) structure factor data

for sulfenyl amide protein tyrosine phosphatase 1B recorded thereon, the structure factor data being derivable from the atomic coordinate data of Table 1 or Table 2 ± root mean square deviation from the Cα atoms of not more than 1.5Å; (c) atomic coordinate data of a target sulfenyl amide protein tyrosine phosphatase protein generated by homology modeling of the target based on the data of Table 1 or Table 2 ± root mean square deviation from the Cα atoms of not more than 1.5Å; (d) atomic coordinate data of a sulfenyl amide protein tyrosine phosphatase 1B-ligand complex or a sulfenyl amide protein tyrosine phosphatase 1B homologue or analogue generated by interpreting X-ray crystallographic data or NMR data by reference to the data of Table 1 or Table 2 ± root mean square deviation from the Cα atoms of not more than 1.5Å; and (e) structure factor data derivable from the atomic coordinate data of (c) or (d).

113. (***new***) A computer-based method of rational drug design which comprises:

providing the structure of the PTP1b sulfenyl amide as defined by the coordinates of Table 1 or Table 2 ± root mean square deviation from the Cα atoms of not more than 1.5Å or selected co-ordinated thereof;

providing the structure of a candidate modulator molecule; and

fitting the structure of candidate to the structure of the sulfenyl amide of Table 1 or Table 2 ± root mean square deviation from the Cα atoms of not more than 1.5Å or selected coordinates thereof.

114. (***new***) A method of identifying by rational drug design a compound capable of reducing the level of activity of a protein tyrosine phosphatase (PTP) in a cellular environment, the PTP being one which is convertible in a cellular environment between an active form and an inactive or less active form, the inactive form or less active form being characterized by the presence of a sulfenyl amide moiety formed at the active site of the PTP between the sulfur atom of a cysteine group and a backbone nitrogen atom of a neighbouring amino acid;

which method comprises:

(a) designing a ligand that will (i) bind to the active site in the region of the sulfenyl amide moiety to inhibit conversion of the inactive form back to the active form, or (ii) modify the sulfenyl amide moiety to inhibit conversion of the inactive form of the PTP to the active form;

(b) synthesizing the ligand; and

(c) determining whether the ligand reduces the level of activity of a protein tyrosine phosphate (PTP) in a cellular environment.

115. (***new***) A method according to claim 114 wherein the protein tyrosine phosphatase is characterized by a signature sequence of the formula: (I/V)HCXAGXXR(S/T/G) at a catalytic site thereof wherein the amino acid C is cysteine 215, and wherein the sulfenyl amide moiety is formed between the sulfur atom of cysteine 215 and a backbone nitrogen atom of a neighbouring amino acid.

116. (***new***) A method according to claim 114 wherein the PTP is PTP1B and the ligand is one which is capable of binding to the sulfenyl amide PTP1B at a first binding site of the sulfenyl amide PTP constituted by a groove lined by residues 41-47 of the phosphotyrosine recognition loop, residues 88-90, 115 to 120, residues 179 to 184 of the WPD-loop, residues 215 to 219 of the phosphate-binding cradle, and residues 262-266 or at a second binding site of the sulfenyl amide PTP constituted by a shallow depression defined by residues of the WPD-loop, the pTyr recognition loop and the loop containing residues 28-32.

117. (***new***) A method for determining the structure of a compound bound to sulfenyl amide PTP1B, said method comprising: (a) providing a crystal of sulfenyl amide PTP1b; (b) soaking the crystal with said compound; and (c) determining the structure of said sulfenyl amide PTP1b compound complex by employing the data of Table 1 or Table 2 ± root mean square deviation from the Cα atoms of not more than 1.5Å.

118. (***new***) A method of inhibiting or preventing the reduction of sulfenyl amide PTB1B to PTB1B in a cellular environment by exposing the PTB1B to a ligand capable of binding to the sulfenyl amide PTB1B in the region of the sulfenyl amide moiety so as to prevent reduction of the sulfenyl amide moiety by an intracellular reducing agent.

119. (***new***) A method for the prevention or treatment of a disease state or condition mediated by PTP such as PTP1B in a patient in need thereof, which method comprises administering to the patient a therapeutically effective amount of a compound designed by the method of claim 114.

120. (***new***) The method of claim 114 further comprising the step of (d) identifying the ligand as an inhibitor on the basis of its ability to prevent or inhibit the reductive activation of the sulfenyl amide to active protein.

121. (***new***) A method for producing a pharmaceutical composition comprising the method of identifying a compound according to claim 120 and further comprising the step of: (e) incorporating the inhibitor identified in step (d) into a pharmaceutical excipient.

122. (***new***) The method for producing a pharmaceutical composition comprising the method of claim 114 and further comprising the step of: (d) incorporating the ligand identified in step (c) into a pharmaceutical excipient.